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 TITLE: Cyclosporin derivatives
 INVENTOR(S): Traber, Rene; Kuhn, Max; Hofmann, Hans; Haerri, Eugen
 P.
 PATENT ASSIGNEE(S): Sandoz-Patent-G.m.b.H., Switz.
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 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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DE 2819094	A1	19781123	DE 1978-2819094	19780429
DE 2819094	C2	19881103		
CH 628022	A	19820215	CH 1977-5822	19770510
CH 628023	A	19820215	CH 1977-5823	19770510
CH 632010	A	19820915	CH 1977-7457	19770617
DK 7801887	A	19781111	DK 1978-1887	19780501
DK 148751	B	19850916		
DK 148751	C	19860224		
FI 7801348	A	19781111	FI 1978-1348	19780502
FI 59814	B	19810630		
FI 59814	C	19811012		
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US 4220641	A	19800902	US 1978-902794	19780504
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AT 7803339	A	19810615	AT 1978-3339	19780509
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CA 1117046	A1	19820126	CA 1978-302914	19780509
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AT 8002465	A	19810915	AT 1980-2465	19800509
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AT 366663	B	19820426		
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FI 63561	C	19830711		
FI 8001682	A	19800526	FI 1980-1682	19800526
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FI 63562	C	19830711		
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SE 8401134	A	19840301	SE 1984-1134	19840301
SE 8401135	A	19840301	SE 1984-1135	19840301

PRIORITY APPLN. INFO.:

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CH 1977-5823	A	19770510
CH 1977-7457	A	19770617
FI 1978-1348	A	19780502
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AT 1978-3339	A	19780509

GI For diagram(s), see printed CA Issue.

AB Cyclosporin D (I) [63775-96-2], dihydrocyclosporin D (II) [63775-91-7], or isocyclosporin D (III) [63775-93-9] is obtained by culturing Tolypocladium inflatum on a nutrient medium. Thus, 500 L of a nutrient solution containing glucose 40, Na caseinate 2.0, ammonium phosphate 2.5, MgSO₄·7H₂O 5.0, KH₂PO₄ 2.0, NaNO₃ 3.0, KCl 0.5, and FeSO₄ 0.01 g/L was inoculated with a seed culture of strain NRRL 8004 in a steel fermentor and incubated with stirring and aeration at 27° for 13 days. Separation and purification procedures resulted in colorless prismatic crystals of I with m.p. 148-51°, [α]_D20 = -245° (c = 0.52 in CHCl₃), and [α]_D20 = -211° (c = 0.51 in MeOH).

IT 63775-91-7P 63775-96-2P

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP
(Preparation)

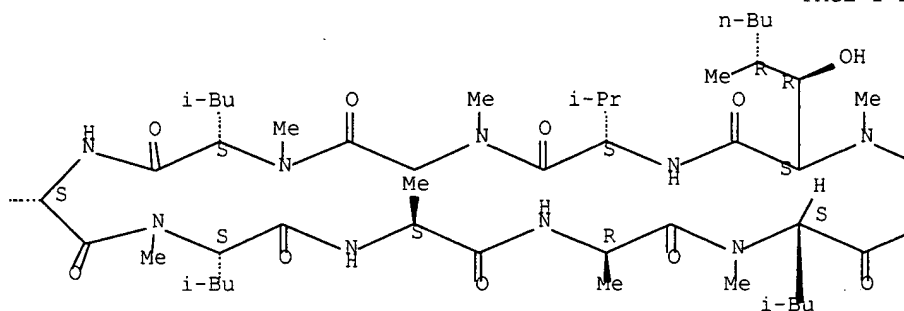
(manufacture of, with Tolypocladium inflatum)

RN 63775-91-7 HCAPLUS

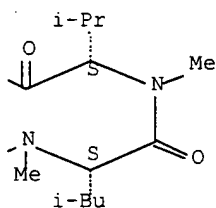
CN Cyclosporin D, 6-[(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)octanoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-C



RN 63775-96-2 HCAPLUS
CN Cyclosporin D (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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